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Multicenter, Randomized, Open-Label Study Comparing the Efficacy and Safety of Micafungin versus Itraconazole for Prophylaxis of Invasive Fungal Infections in Patients undergoing Hematopoietic Stem Cell Transplant

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This multicenter, randomized, open-label phase III study compared the efficacy and safety of micafungin and itraconazole in prophylaxis of invasive fungal infections in neutropenic patients undergoing hematopoietic stem cell transplants in China. Micafungin (50 mg/day i.v.) or itraconazole (5 mg/kg/day p.o.) was administered for ≤42 days. The primary endpoint, treatment success, was defined as no proven, probable, or suspected invasive fungal infection through therapy and the absence of proven or probable invasive fungal infection through the end of 4 weeks after therapy. Noninferiority of micafungin against itraconazole was established if the lower boundary of the 95% confidence interval (CI) was >10%. Of 287 patients, 283 were evaluable for efficacy (136 for micafungin, 147 for itraconazole, intent-to-treat population). Treatment success was documented in 92.6% (126 of 136) of micafungin-treated patients and 94.6% (139 of 147) of itraconazole-treated patients (95% CI, −7.562% to 3.482%; $P = .48$), indicating noninferiority of micafungin against itraconazole. Results were similar for patients treated per protocol. Whereas the rates of proven or probable invasive fungal infection were numerically higher with micafungin than itraconazole at 4.4% (6 of 136) and 1.4% (2 of 147), rates of suspected invasive fungal infection were similar at 5.9% (8 of 136) and 7.5% (11 of 147), respectively. More patients treated with micafungin than itraconazole completed the study (82.9% versus 67.3%, respectively). Significant differences in incidence of withdrawal due to an adverse event (4.4% versus 21.1%) and drug-related adverse events (8% versus 26.5%) were shown between micafungin and itraconazole ($P = .00$, chi-square test). Micafungin was as effective as itraconazole in preventing invasive fungal infections in patients with neutropenia. In comparison to itraconazole, treatment tolerance was much better with micafungin.

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KEY WORDS: Micafungin, Itraconazole, Prevention of invasive fungal infection, Antifungal prophylaxis, Hematopoietic stem cell transplant

INTRODUCTION

Candida and *Aspergillus* species fungal infections occur early in the pre-engraftment phase after hematopoietic stem cell transplant (HSCT). Infection is a primary cause of death in HSCT recipients, with a fatality rate of 50% from invasive aspergillosis in patients with neutropenia alone and 86% in patients who are neutropenic after conditioning for HSCT. Because treatment of an established fungal infection is difficult,

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prophylactic treatment with antifungal agents is commonly used in high-risk patients.

Fluconazole is the most widely used antifungal agent and it is recommended for prophylaxis of *Candida* infections for HSCT recipients during the period of neutropenia until engraftment. *Candida* resistance to fluconazole has emerged and fluconazole lacks activity against molds including *Aspergillus*. In contrast to fluconazole, the broad-spectrum triazole, itraconazole, has shown activity against *Aspergillus* species or other molds in HSCT recipients [1,2].

By comparison, the echinocandin micafungin, which exerts its antifungal activity by inhibiting the production of beta-1,3-glucan, has shown antifungal activity against both *Candida* and *Aspergillus* species. In a randomized, double-blind study, the effectiveness of micafungin in providing prophylaxis against proven, probable, or suspected systemic fungal infection in HSCT recipients was significantly higher than the gold standard, fluconazole (80% versus 74%, respectively; $P = .03$) [3]. The use of micafungin has proven to be effective, safe, and well-tolerated [4] with few known drug interactions [5], which are important considerations when implementing antifungal prophylaxis in HSCT recipients.

Itraconazole is currently the only agent for prophylaxis of invasive fungal infections approved by the State Food and Drug Administration in China. A direct comparison of the efficacy and safety of micafungin against itraconazole for antifungal prophylaxis in HSCT recipients, as reported in a randomized clinical trial, could not be identified before designing this study.

The objective of this randomized, controlled, clinical study was to compare the treatment success of micafungin and itraconazole in preventing invasive fungal infections during prophylactic therapy and up to 4 weeks after discontinuation of prophylaxis antifungal therapy in HSCT recipients. The safety and tolerability of each treatment were assessed.

METHODS

Study Design

This was an open, randomized, phase III, multicenter, parallel group study to evaluate and compare the efficacy and safety of micafungin and itraconazole for prophylaxis of invasive fungal infection in patients undergoing HSCT. The duration of the study was 10 weeks. Study procedures were reviewed and approved by the institutional review boards at each of the 10 study centers in China. Conduct of the study was in accordance with the ethical principles that have their origins in the Declaration of Helsinki.

Randomization to the study medication group (micafungin) or to the control group (itraconazole) was 1:1 by block randomization using randomization codes generated by SAS PROC Plan. The randomization table was developed by Excel Pharma Studies, Inc. (Beijing, China). Randomization was stratified by patient age (18-49 and $\geq$50 years) and type of stem cell transplant (SCT).

Patients

Eligible for the study were adult patients, 18 to 70 years old, undergoing allogeneic or autologous HSCT for treatment of a malignancy. Patients were free of liver disease (serum glutamic oxaloacetic or pyruvic transaminase greater than 5 times the normal value, total bilirubin >2.5 times the normal value), the existence of active, deep, or disseminated fungal infection, and known allergy to azoles or echinocandin antifungal agents. Patients were excluded if they had received any antifungal therapy within 72 hours of the first dose of the study drug. Written informed consent was provided before randomization.

Intervention

The study drug, micafungin (Astellas Pharma Inc., Deerfield, IL) was administered i.v. at a dose of 50 mg/day. The control drug, itraconazole (Janssen Pharmaceuticals, Inc., Titusville, NJ) was administered as a solution taken orally at a dose of 5 mg/kg/day (in 2 administrations). Patients were to receive the assigned therapy during the neutropenic (ie, pre-engraftment) phase of HSCT, starting within 48 hours of the beginning of the transplant-related conditioning regimen until the earliest of the following: $\leq$5 days after engraftment (defined as an absolute neutrophil count of $\geq$500 cells/mm^3 after the nadir absolute count); treatment day 42 after HSCT; development of proven, probable, or suspected invasive fungal infection; development of unacceptable drug toxicity; death; withdrawal from study participation (patient's decision); or discontinuation of study treatment (investigator's decision).

Outcomes

Patients were evaluated at baseline, during prophylactic treatment, at the end of treatment, and at 4 weeks after prophylactic treatment, as depicted in the study flow chart (Figure 1). The primary endpoint, treatment success, was defined as the absence of proven, probable, or suspected systemic fungal infection through the end of prophylactic therapy and as the absence of a proven or probable systemic fungal infection through the end of the 4-week posttreatment period. Both criteria must have been fulfilled to achieve treatment success.

According to the Chinese criteria for invasive fungal infection diagnosis [6], proven infection was defined as biopsy-proven invasive or disseminated

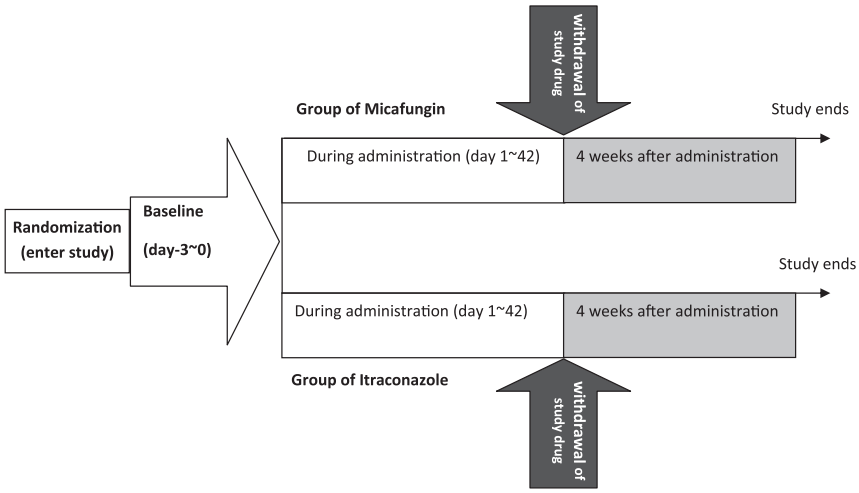


Figure 1. Study flow diagram.

infection. Probable pulmonary aspergillosis was documented if bronchoscopy with bronchoalveolar lavage revealed fungal elements in conjunction with compatible clinical and computerized tomography findings. An invasive fungal infection was defined as suspected if fever (temperature $\geq$38.5°C) persisted for >96 hours during the neutropenic phase, despite broad-spectrum antibacterial therapy, and led to the initiation of empirical antifungal therapy.

The secondary endpoints were the incidence of proven, probable, or suspected invasive fungal infection through the end of prophylactic therapy (treatment failure); the incidence of proven or probable invasive fungal infection at any time during the study; the incidence of proven, probable, or suspected invasive fungal infection after prophylactic therapy in patients who did not have a fungal infection during prophylaxis therapy; incidence by organism of invasive fungal infection; incidence of suspected fungal infection during the study; the rate of use of antifungal agents during the 4 weeks after study medication administration; time to treatment failure; time to suspected invasive fungal infection; incidence of superficial fungal infections during active antifungal treatment; incidence of fungal colonization at baseline and at the end of prophylactic therapy; or patient survival. Safety assessments included adverse event reporting, results of clinical laboratory tests, and vital signs. Hematology and serum chemistry analyses and fungal surveillance cultures were performed at the study sites at baseline, at least twice weekly during the administration of antifungal therapy, and on the final day of prophylactic therapy.

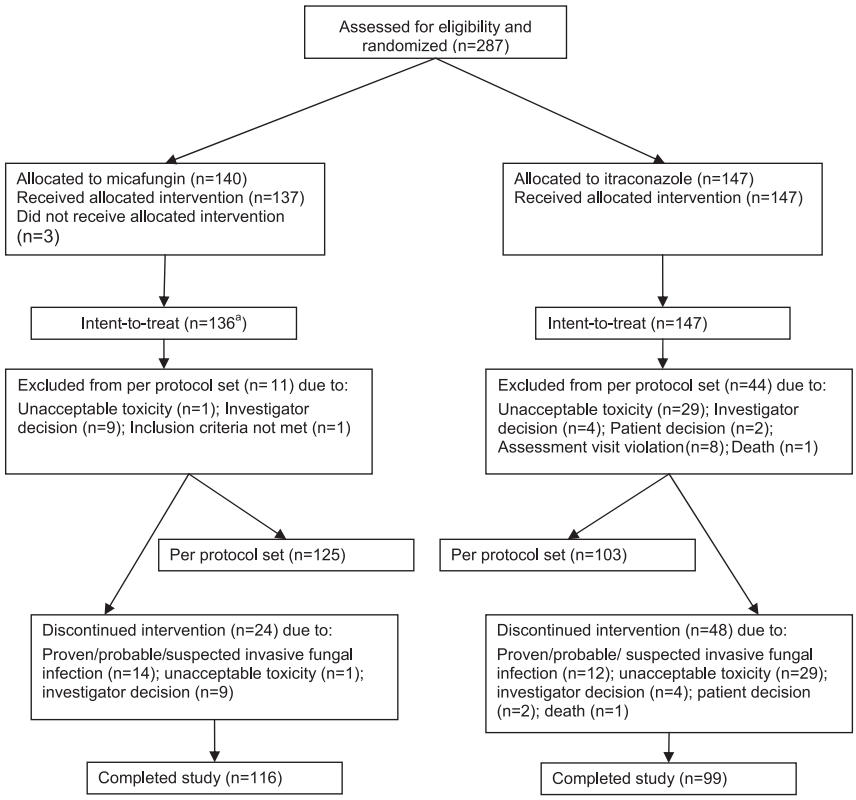
Temperature was monitored on a daily basis. Evaluation of the patient for fungal infection, fungal cultures of the oropharynx, urine, and perirectum or stool, and radiographic scans of the chest were conducted at baseline, on a weekly basis during prophylactic therapy, on the last day of prophylactic therapy, and at 4 weeks after discontinuation of prophylactic therapy.

Statistical Analysis

Data were analyzed for the intent-to-treat population (all patients who had taken at least 1 dose of prophylactic antifungal therapy and had at least 1 endpoint measurement after administration of antifungal therapy) and for the per protocol set (all patients treated per protocol without major protocol deviations). The primary efficacy analysis was based on the intent-to-treat population and on the per protocol set. The safety set (all patients who had taken at least 1 dose of prophylactic antifungal therapy) was used for the analysis of safety data. Efficacy results are presented for the intent-to-treat population, unless noted otherwise, and safety results are presented for the safety set.

For the primary analysis of treatment success, micafungin was considered not to be statistically inferior to itraconazole if the 95% lower confidence boundary on the difference in success rates between micafungin and itraconazole was more than -10%. Micafungin was considered superior to itraconazole if the lower boundary was greater than 0%. The Cochrane-Mantel-Haenszel chi-square test was used to test the difference in distribution between treatment groups. The rate of treatment success was analyzed by stratification of patient age (18-49 and $\geq$50 years) and type of HSCT. The level of significance was 2.5% for the 1-sided test; confidence intervals (CIs) were 2-sided at the 95% level. Data missing for the primary endpoint were imputed using the last observation carried forward and observed case methods.

Secondary endpoints were analyzed using the Cochrane-Mantel-Haenszel test. Time to treatment



[a] One patient randomized to micafungin was excluded from the intent-to-treat population because of not meeting inclusion criteria; this patient received one dose of study drug and is therefore included in the safety set.

Figure 2. Patient flow through the study.

failure and time to suspected invasive fungal infection were analyzed by stratified log-rank test using age and type of HSCT as covariates.

Sample Size

Based on a 1:1 randomization, an estimated 240 patients were required to reach a power of 80% to show that the rate of treatment success for micafungin is not <10% compared to itraconazole. The Chinese State Food and Drug Administration require a minimum of 100 patients to be enrolled in each arm of a clinical study; it was therefore decided to enroll 125 patients in each treatment group.

RESULTS

Patients

Patient data were collected between November 2008 and November 2009. A total of 287 patients were enrolled and randomized (block randomization resulted in an unequal number of patients allocated to each treatment group; Figure 2). Of the randomized patients, 136 and 147 patients received 1 dose of micafungin or itraconazole, respectively, and had at least 1 endpoint measurement after receiving treatment; data from these patients were used to determine the primary endpoint in the intent-to-treat population. For the determination of the primary endpoint using patients treated per protocol, data from 125 micafungin-treated patients and 103 itraconazole-treated patients were available.

Both groups were broadly comparable at baseline (Table 1). The age range of patients was 18 to 58 years. Most commonly, patients in both groups received HSCT for treatment of acute lymphocytic leukemia (16% in both groups), acute myeloid leukemia (19% in both groups), or chronic myeloid leukemia (14% in both groups). The duration of neutropenia was similar between the 2 arms (15 days in both groups), but it was significantly different between autologous versus allogeneic transplant recipients, being much shorter in the autologous transplant group.

The mean (SD) duration of prophylactic antifungal treatment was similar at 25 days (6.5) in the micafungin group and 22.1 days (7.7) in the itraconazole group.

Treatment Outcome

There were no statistically significant or clinically meaningful differences between treatments in the rate of patients without proven, probable, or suspected

Table 1. Baseline and Demographic Characteristics of Recipients of SCT

	Intent-to-treat population	
	Micafungin (n = 136)	Itraconazole (n = 147)
Gender		
Male, n (%)	87 (64)	94 (63.9)
Female, n (%)	49 (36)	53 (36.1)
Age		
Mean (SD), yr	32.1 (10.1)	33.3 (10.5)
18-49 yr, n	127	134
≥50 yr, n	9	13
Transplant type		
Autologous transplant, n (%)	24 (17.6)	32 (21.8)
Allogeneic transplant, n (%)	112 (82.4)	115 (78.2)
Period of neutropenia		
Recovery achieved, n	121	130
Overall, median days (range)	15.0 (3-47)	15.0 (3-50)
Autologous transplant, median days (range)	8.5 (4-41)	8.0 (4-23)
Allogeneic transplant, median days (range)	15.0 (3-47)	17.0 (3-50)

SCT indicates stem cell transplant.

invasive fungal infection during prophylactic antifungal treatment and without proven or probable invasive fungal infection after completion of prophylactic treatment (treatment success; Table 2). The difference between the groups as determined by analysis of the intent-to-treat was −2.04% with a 95% CI of −7.562% to 3.482% (P = .48). Outcomes in the 2 groups were similar using the per protocol set: the difference between treatments was −0.861% (95% CI, −7.489% to 5.767%). The analyses of the difference between therapies in both the intent-to-treat and per protocol populations showed that the lower boundary of the 95% CI was >−10%, thereby demonstrating the noninferiority of micafungin over itraconazole.

Neither patient age nor type of SCT had an impact of clinical meaning on differences between the 2 treatments in the rate of patients without proven, probable, or suspected invasive fungal infection (Table 2).

As shown in Table 3, there were no differences of clinical meaning between micafungin and itraconazole in the incidence of proven, probable, or suspected invasive fungal infections occurring during prophylactic therapy, after therapy, or at any time during the study. The incidence of fungal infections occurring during prophylactic treatment with either micafungin or itraconazole (treatment failure) was comparable at 7.4% and 5.4%, respectively. The time to treatment failure was also similar; Kaplan-Meier analysis showed no significant difference between the treatments (P = .51) nor was a significant difference found using Cox regression analysis (P = .52; hazard proportion 0.74 [95% CI, 0.29% to 1.86%]).

One proven and 1 probable infection with *Candida* were reported in the micafungin group. One probable *Aspergillus* infection occurred in the itraconazole group. All these infections occurred during prophylactic treatment. One case of superficial fungal infection was reported in the micafungin group.

There were no cases of proven or probable fungal infection occurring after completion of prophylactic treatment reported in patients who remained free of infection during prophylactic treatment. A suspected fungal infection, however, was reported in 4 of 126 micafungin-treated patients (3.2%) and in 5 of 139 (3.6%) itraconazole-treated patients after completion of prophylactic treatment.

The use of systemic antifungal agents after prophylactic administration of micafungin and itraconazole was similar in the 2 treatment groups. In the micafungin group, 25.8% of patients (34 of 136 patients) received antifungal therapy, and in the itraconazole group, the rate was 24.3% of patients (35 of 147 patients).

Colonization

Colonization at baseline was similar, with *C. albicans* accounting for 0.7% of isolates in both treatment groups. At the end of prophylactic therapy, *C. albicans* was recovered from any site from 5.1% of micafungin-treated patients (7 of 136 patients) and in no itraconazole-treated patients. Incidents of colonization with *C. glabrata* were low and similar between micafungin-treated and itraconazole-treated patients at 1.5% (2 of 136 patients) and 1.4% (2 of 147 patients), and colonization with *C. tropicalis* was comparable at 0.7% in both groups (1 patient in each group). The

Table 2. Absence of Invasive Fungal Infections in All Patients and in Prespecified Subgroups

	Intent-to-treat population		Per protocol set	
	Micafungin (n = 136)	Itraconazole (n = 147)	Micafungin (n = 125)	Itraconazole (n = 103)
No invasive fungal infection*	126 (92.6)	139 (94.6)	115 (92)	96 (93.2)
	95% CI, −7.562 to 3.482		95% CI, −7.489 to 5.767	
Age, 18-49 yr	118/127(92.9)	126/134 (94)	108/117 (92.3)	85/92 (92.4)
Age, ≥50 yr	8/9 (88.9)	13/13 (100.0)	7/8 (87.5)	11/11 (100)
Autologous transplant	22/24 (91.7)	32/32 (100)	18/20 (90)	23/23 (100)
Allogeneic transplant	104/112 (92.9)	107/115 (93)	97/105 (92.4)	73/80 (91.3)

CI indicates confidence interval.

*No proven, probable, or suspected invasive fungal infection during prophylactic antifungal treatment and no proven or probable invasive fungal infection after completion of prophylactic treatment.

Table 3. Incidence of Proven, Probable, or Suspected Invasive Fungal Infection

	Intent-to-treat population		Per protocol set	
	Micafungin (n = 136)	Itraconazole (n = 147)	Micafungin (n = 125)	Itraconazole (n = 103)
Infection during prophylactic treatment (treatment failure)	10 (7.4)	8 (5.4)	10 (8)	7 (6.8)
Proven infection	1 (0.7)	0	1 (0.8)	0
Aspergillosis	0	0	0	0
Candidiasis	1 (0.7)	0	1	0
Probable infection	5 (3.7)	2 (1.4)	5 (4)	2 (1.9)
Aspergillosis	0	1	0	1
Candidiasis	1	0	1	0
No mycological criterion	4	1	4	1
Suspected infection	4 (2.9)	6 (4.1)	4 (3.2)	5 (4.9)
Time to treatment failure, mean (SD), days	21.3 (6.1)	19.8 (6.7)	21.3 (6.1)	20.4 (6.9)
Infection after prophylactic treatment	4 (2.9)	5 (3.4)	4 (3.2)	5 (4.9)
Proven infection	0	0	0	0
Probable infection	0	0	0	0
Suspected infection	4 (2.9)	5 (3.4)	4 (3.2)	5 (4.9)
Infection at any time during the study	14 (10.3)	13 (8.8)	14 (11.2)	12 (11.7)
Proven infection	1 (0.7)	0	1 (0.8)	0
Probable infection	5 (3.7)	2 (1.4)	5 (4)	2 (1.9)
Suspected infection	8 (5.9)	11 (7.5)	8 (6.4)	10 (9.7)

Data are presented as n (%) unless otherwise indicated.

classification of isolate was recorded as unknown in 1.5% (2 patients) of cases in the micafungin group. The oropharynx was the most common site of colonization in the micafungin group (9 of 12 cases), followed by the perirectum (2 cases) and in urine (1 case). The perirectum/stool was the site of all 3 cases of colonization in the itraconazole group.

Safety

There was 1 patient death in the itraconazole group. The cause of death was pneumonia.

Tolerability of treatment was better in the micafungin group, with more patients in that group completing the study (82.9% versus 67.3%) and a significantly lower incidence of premature study withdrawal due to an unacceptable toxicity (0.7% versus 19.7%; $P = .00$, chi-square test) occurring in micafungin-treated versus itraconazole-treated patients. Patients withdrawn due to adverse events received an alternative regimen, such as itraconazole i.v. formulation, fluconazole, voriconazole, or caspofungin.

Study drug administration was interrupted because of adverse events for 2 itraconazole patients (1.4%). The reasons for interrupting itraconazole were hemolysis and gastrointestinal disorders (nausea, vomiting, and diarrhea).

Adverse events were reported in significantly fewer patients in the micafungin than in the itraconazole group. Whereas the overall incidence of an adverse event was 43.8% (60 of 137 patients) in micafungin-treated patients, the incidence was 56.5% (83 of 147 patients) in the itraconazole group ($P = .033$, chi-square test). There was also a significant difference in the rate of investigator-identified, drug-related adverse events, which was 8.0% in micafungin-treated patients (11 of 137 patients) and 26.5% in itraconazole-treated patients (39 of 147 patients; $P = .000$, chi-square test; Table 4). No serious drug-related adverse events were reported in either group.

Serum creatinine increased slightly between baseline and 4 weeks after prophylactic therapy in micafungin-treated patients and decreased slightly in itraconazole-treated patients. The change in median (range) values in the micafungin group was 4.1 (−30 to 121) mg/dL, and in the itraconazole group it was −6.0 (−59 to 169) mg/dL. Values for total bilirubin and BUN remained unchanged in both groups. Alanine transaminase remained relatively stable with micafungin (median [range] 1.0 [−164 to 317] IU/L) but increased during the study with itraconazole (5.0 [−109 to 284] IU/L).

Table 4. Adverse Events by Study Group, Safety Set

	Micafungin (n = 137)	Itraconazole (n = 147)	*P* value*
Any event	60 (43.8)	83 (56.5)	.033
Events with an incidence ≥3%			
Diarrhea	8 (5.8)	14 (9.5)	
Gastrointestinal disorder (not classified)	12 (8.8)	22 (15)	
Nausea	8 (5.8)	19 (12.9)	.042
Vomiting	7 (5.1)	17 (11.6)	.051
Pyrexia	23 (16.8)	20 (13.6)	
Hyponatremia	6 (4.4)	1 (0.7)	
Abnormal liver function test	9 (6.6)	7 (4.8)	
Increased transaminase	5 (3.6)	9 (6.1)	
Any drug-related event	11 (8.0)	39 (26.5)	.000
Events with statistical difference			
Gastrointestinal disorder	0 (0)	12 (8.2)	.001
Nausea	0 (0)	9 (6.1)	.004
Vomiting	0 (0)	8 (5.4)	.007

Data are presented as n (%). Safety set: patients who had taken at least 1 dose of prophylactic antifungal therapy.
*Chi-square test.

DISCUSSION

This randomized study demonstrates the efficacy of micafungin for antifungal prophylaxis in patients with neutropenia. The rate of treatment success was similar for micafungin and itraconazole in this population of patients with neutropenia.

Our study compared the efficacy and safety of micafungin with that of itraconazole for prevention of invasive fungal infection during neutropenia by means of a design similar to that used by van Burik et al. [3], which compared micafungin with fluconazole. In that study, the overall rate of treatment success was significantly higher for patients treated with micafungin (80%) than for patients treated with flucaonzole (73.5%; 95% CI, 0.9%-12%; $P = .03$). In the study by van Burik et al. [3], which included adult and pediatric patients, the treatment success in adults was much better than that in the pediatric population. However, in our study, only adult patients were included. This should be taken into consideration when comparing the overall treatment success between the 2 studies. The results we report for treatment success provide evidence for the noninferiority of micafungin over itraconazole in preventing invasive fungal infections in HSCT recipients. Even when the duration of neutropenia is taken into account, the results do not change.

However, in a post-hoc analysis, in which a composite endpoint (no breakthrough fungal infections, survival 7 days after the end of therapy, and no discontinuation due to toxicity or lack of efficacy before recovery from neutropenia) for treatment success was used, the results for the micafungin group are significantly better than those for the itraconazole group (91.9% [125 of 136] versus 74.1% [109 of 147]). In our study, 29 patients were withdrawn due to toxicity in the itraconazole group, whereas there was just 1 patient in the micafungin group, this being the most important reason for the marked difference.

Colonization with *Candida* species was 3-fold higher in the micafungin than in the itraconazole group, and the most common site of colonization was the oropharynx in micafungin-treated patients. The reason for this difference is unclear as micafungin has demonstrated potent activity in vitro and in vivo against all *Candida* species [7,8]. We speculate that the oral solution formulation of itraconazole might have provided greater benefit than the parenteral formulation of micafungin in terms of preventing oropharyngeal colonization.

The efficacy results of our study compare favorably with those from 2 other studies of similar design, although we administered micafungin at a lower daily dose. We administered micafungin at a dose of 50 mg/day, and our rate of treatment success was about 93%. In comparison, in 2 studies conducted in Japan, Hashino et al. [9] achieved an 88% rate of treatment success by administering micafungin at double our daily dose (100 mg/day), and Hiramatsu et al. [10] achieved a similar rate of treatment success (94%) by administering micafungin at a substantially higher daily dose (150 mg/day). At the same daily dose, the rate of treatment success we found was higher than that reported in the much larger randomized study conducted by van Burik et al. [3].

The protocol-specified duration of prophylactic antifungal treatment was ≤42 days, but the actual length of treatment was much shorter in both groups at approximately 23 days. No cases of proven or probable invasive fungal infection, only suspected cases, occurred in either group after the administration of prophylactic therapy. Of interest, empirical antifungal therapy was administered to approximately one-quarter of patients in each group. We did not collect information on the reason for the administration of empirical therapy.

Antifungal prophylaxis is recommended for patients undergoing HSCT. Data from meta-analyses of randomized studies indicate reductions in fungal-related mortality, reductions in documented invasive fungal infections, and reductions in empiric parenteral antifungal therapy in patients who underwent HSCT treated with antifungal prophylaxis [11,12]. Conflicting evidence exists over whether or not antifungal prophylaxis positively impacts on mortality from all causes. As we had a low number of deaths and no deaths attributable to fungal infections, our results would support a positive impact of antifungal therapy on infection-related morbidity.

The benefit of prophylactic antifungal therapy should outweigh any risk of adverse drug effects [13]. The results of this study provide further evidence for the better patient tolerability of micafungin over itraconazole. The incidence of adverse events, events leading to premature study discontinuation, and events causing discontinuation of the study drug were significantly higher with itraconazole. Unfortunately, the benefits of treatment with itraconazole are offset by poor patient tolerance, and toxicity associated with the solution formulation [1,2] and drug discontinuation, especially due to nausea, is high [14].

CONCLUSION

The results of this comparative study showed that micafungin was as effective as itraconazole in preventing invasive fungal infection in recipients of a hematopoietic SCT. Lower incidents of adverse events and premature study withdrawal indicate better patient tolerability of antifungal treatment with micafungin over itraconazole.

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